

E.1

MULTIPLE DONOR POOLED CRYOPRESERVED HUMAN HEPATOCYTES

Multi-donor hepatocyte pools are designed for use in metabolism studies and save time and money by eliminating the need for pooling by the customer and using one pooled vial instead of multiple individual vials. The pools are produced from CellzDirect's extensive inventory of superior human cryopreserved hepatocytes.

Quality and Characterization

We have carefully produced and characterized our lots, offering detailed donor demographics, extensive P450 profiling, morphological assessment, and application suitability. The commonly tested Phase I (P450) and Phase II drug metabolizing enzymes were analyzed for activity in each of our lots. Metabolite formation was measured by standard biochemical assays using GLP validated LC-MS/MS assays.

Preparation and Thawing

In order to obtain reliable and consistent results from your cryopreserved hepatocytes assays, it is critical to focus on preparing healthy cells for incubation. CellzDirect provides detailed instruction for thawing and using cryopreserved hepatocytes. To maximize cell yield, the use of our standard procedure is recommended. To maximize cell viability thawing using CellzDirect's Cryopreserved Hepatocyte Recovery Medium (CHRM) is recommended.

Pools – Catalog # HMCH-M8-P10

Lot #: HuP50

Donor Information	Yield	% Viability	ECOD	7-HCG	7-HCS	pmol/l x 10 ⁶ cells/min							
						CYP 3A4 (TES)	CYP 3A4 (MDZ)	CYP 1A2	CYP 2B6	CYP 2C8	CYP 2C9	CYP 2C19	CYP 2D6
10-Donor 5-male/5-Female Ages 17-59	5 Million Cells/Vial	87%	40	593	21	784	N/A	138	N/A	6	81	16	35

Lot #: HuP58

Donor Information	Yield	% Viability	ECOD	7-HCG	7-HCS	pmol/l x 10 ⁶ cells/min							
						CYP 3A4 (TES)	CYP 3A4 (MDZ)	CYP 1A2	CYP 2B6	CYP 2C8	CYP 2C9	CYP 2C19	CYP 2D6
10-Donor 5-male/5-Female Ages 17-59	5 Million Cells/Vial	81%	21	600	33	567	125	38	43	34	83	82	16

Lot #: HuP59

Donor Information	Yield	% Viability	ECOD	7-HCG	7-HCS	pmol/l x 10 ⁶ cells/min							
						CYP 3A4 (TES)	CYP 3A4 (MDZ)	CYP 1A2	CYP 2B6	CYP 2C8	CYP 2C9	CYP 2C19	CYP 2D6
10-Donor 5-male/5-Female Ages 14-74	5 Million Cells/Vial	90%	35	777	33	567	187	98	59	32	91	26	21

Lot #: HuP60

Donor Information	Yield	% Viability	ECOD	7-HCG	7-HCS	pmol/l x 10 ⁶ cells/min							
						CYP 3A4 (TES)	CYP 3A4 (MDZ)	CYP 1A2	CYP 2B6	CYP 2C8	CYP 2C9	CYP 2C19	CYP 2D6
10-Donor 5-male/5-Female Ages 20-75	5 Million Cells/Vial	89%	28	975	42	475	68	49	49	13	80	9	20

NOTES:

Viability and cell yield was produced using the CHRM thawing method. Viability and cell yield using Williams' medium E (WEM) is also available.

Target post-thaw yield is 5 million viable cells per vial unless noted.

CYP2C8 = Paclitaxel 6 α -Hydroxylation

7-HCG = 7-hydroxycoumarin glucuronide (Phase II metabolism)

7-HCS = 7-hydroxycoumarin sulfate (Phase II metabolism)

CYP2B6 = Bupropion Hydroxylation

*Average post-thaw viability based on CellzDirect, Inc. thawing protocol

ECOD = 7-ethoxycoumarin-O-deethylation (General Phase I metabolism)

CYP1A2 = Phenacetin O-Deethylation

CYP2C9 = Diclofenac 4'-Hydroxylation

CYP2C19 = Mephenytoin 4'-Hydroxylation

CYP2D6 = Dextromethorphan O-Deethylation

CYP3A4 = Testosterone 6 β -Hydroxylation

CYP3A4 = Midazolam 1'-Hydroxylation

TEL: 866.95.CELLZ (23559)

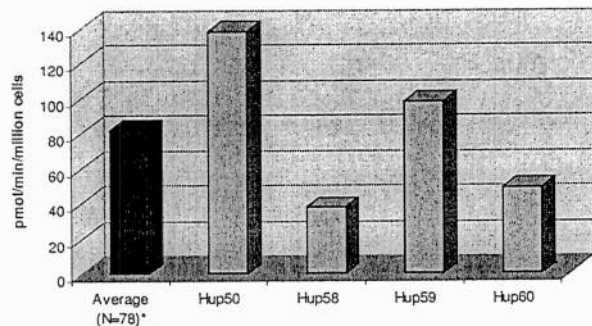
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CellzDirect™

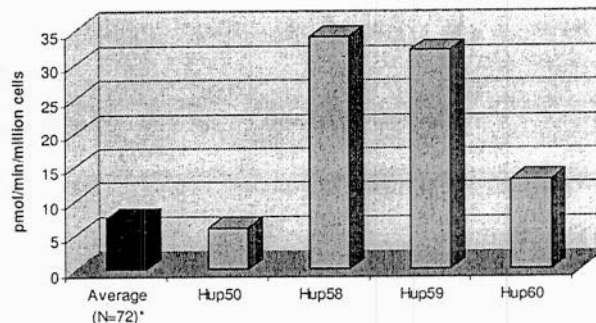
ENZYMATIC ACTIVITY FOR MULTIPLE DONOR POOLS

Average* = Observed data from internal study using single donor lots

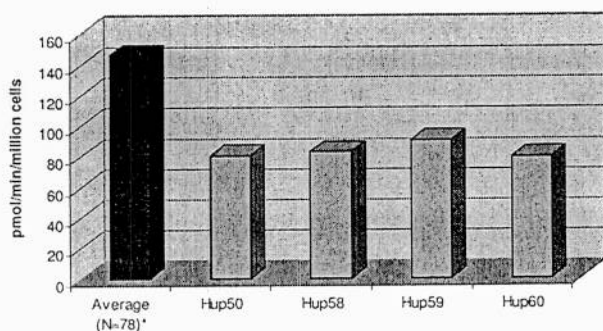
CYP1A2 (Phenacetin O-Deethylation)



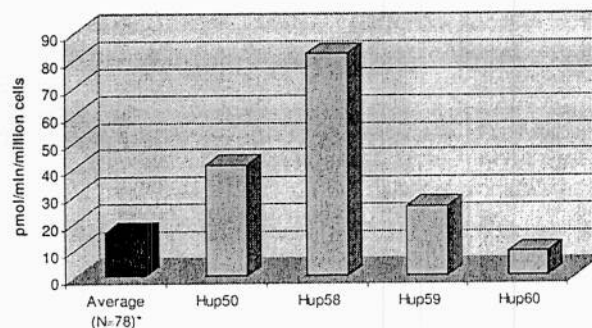
CYP2C8 (Paclitaxel 6 α -Hydroxylation)



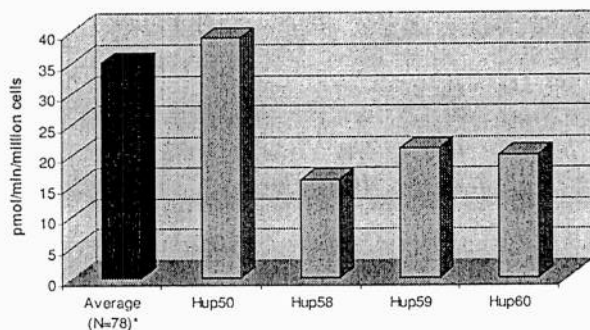
CYP2C9 (Diclofenac 4'-Hydroxylation)



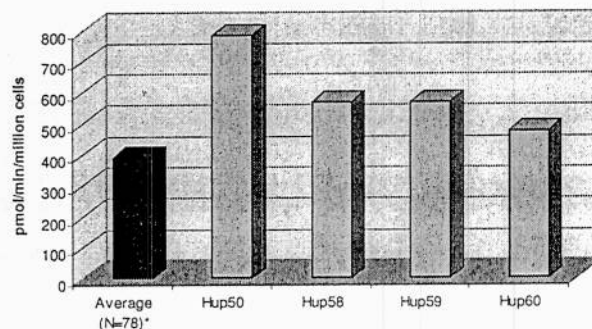
CYP2C19 (Mephenytoin 4'-Hydroxylation)



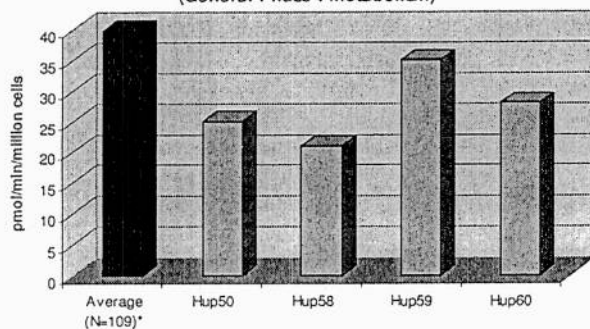
CYP2D6 (Dextromethorphan O-Deethylation)



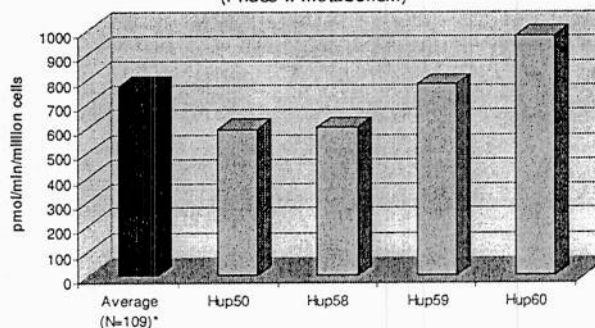
CYP3A4 (Testosterone 6 β -Hydroxylation)



**ECOD (7-ethoxycoumarin-O-deethylation)
(General Phase I metabolism)**



**7-HCG (7-hydroxycoumarin glucuronide)
(Phase II metabolism)**



TEL: 866.95.CELLZ (23559)

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CellzDirect™

E.2



CellzDirect™ Hepatic Products List

CellzDirect, a globally-recognized leader in hepatic tissue sourcing, cell isolation and ADME *in vitro* services, carries a comprehensive line of hepatic products to advance your *in vitro* DMPK research:

- Fresh primary hepatocytes from major toxicology species, including human
- Cryopreserved primary hepatocytes from major toxicology species, including human
- Liver subcellular fractions, such as microsomes, S9 and cytosol
- GenoMembrane™ transporter inside-out vesicles and membranes
- B-CLEAR® kits for the evaluation of biliary excretion
- Media formulated for the thawing and plating of cryopreserved hepatocytes

Two ways to order: CellzDirect or Invitrogen

Starting mid-July 2009, you can purchase cryopreserved hepatocytes and liver subcellular fractions through either CellzDirect or Invitrogen. For availability through Invitrogen, check out the website at www.invitrogen.com/hepatocytes or call your local Invitrogen Customer Services team. Freshly isolated hepatocytes, currently sold exclusively in North America, are only available through CellzDirect.

Technical support

For support selecting the appropriate lot of cryopreserved hepatocytes for your research applications, accessing protocols, or tracking orders placed through CellzDirect, please contact our hepatic biology technical support team.

Americas

Email: hepaticproducts@invitrogen.com
Toll-free Tel: +1 866 952 3559
Tel: +1 919 237 4500
Fax: +1 866 902 3559

Europe

Email: hepaticproducts@invitrogen.com
Tel: +44 141 814 5900
Fax: +44 141 626 6954

Asia-Pacific

Email: hepaticbiology@invitrogen.com
Tel (US-based): +1 919 237 4500

Cryopreserved primary hepatocytes

- Functionally-tested for relevant CYP450, Phase I and Phase II enzyme activities
- Available in single donor as well as convenient, ready-to-use, pooled lots
- Cryopreserved to retain high viabilities and liver-like phenotypes
- Human lots are pre-tested and selected for their ideal application

Hepatic Products List

Product	Concentration	Quantity	Cat. no.
Human plateable cryopreserved hepatocytes (Please check the lot's certificate of analysis for exact cell count.)			
Human Plateable Hepatocytes, Transporter Qualified	4–8 million viable cells/mL	1.0 mL	HMCP1S
Human Plateable Hepatocytes, Transporter Qualified	9–12 million viable cells/mL	1.0 mL	HMCP1L
Human Plateable Hepatocytes, Induction Qualified	4–8 million viable cells/mL	1.0 mL	HMCP1S
Human Plateable Hepatocytes, Induction Qualified	9–12 million viable cells/mL	1.0 mL	HMCP1L
Human Plateable Hepatocytes, Metabolism Qualified	4–8 million viable cells/mL	1.0 mL	HMCP1S
Human Plateable Hepatocytes, Metabolism Qualified	9–12 million viable cells/mL	1.0 mL	HMCP1L
Human suspension cryopreserved hepatocytes			
Human Suspension Hepatocytes, Metabolism Qualified, Male	4–8 million viable cells/mL	1.0 mL	HMCS1S
Human Suspension Hepatocytes, Metabolism Qualified, Male	9–12 million viable cells/mL	1.0 mL	HMCS1L
Human Suspension Hepatocytes, Metabolism Qualified, Female	4–8 million viable cells/mL	1.0 mL	HMCS2S
Human Suspension Hepatocytes, Metabolism Qualified, Female	9–12 million viable cells/mL	1.0 mL	HMCS2L
Human Suspension Hepatocytes, Metabolism Qualified, Pooled Donors	4–8 million viable cells/mL	1.0 mL	HMCS3S
Human Suspension Hepatocytes, Metabolism Qualified, Pooled Donors	9–12 million viable cells/mL	1.0 mL	HMCS3L
Human Suspension Hepatocytes, Polymorphic Donors	4–8 million viable cells/mL	1.0 mL	HMCS1S
Human Suspension Hepatocytes, Polymorphic Donors	9–12 million viable cells/mL	1.0 mL	HMCS1L
Animal suspension and plateable cryopreserved hepatocytes (Please inquire for minipig, guinea pig, and other custom species.)			
Dog (Beagle) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	DGCS10
Dog (Beagle) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	DGCS20
Dog (Beagle) Cryopreserved Hepatocytes, Plateable Male	4–8 million viable cells/mL	1.0 mL	DGCP10
Dog (Beagle) Cryopreserved Hepatocytes, Plateable Female	4–8 million viable cells/mL	1.0 mL	DGCP20
Fish (Rainbow Trout) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	TRCS10
Fish (Rainbow Trout) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	TRCS20
Fish (Rainbow Trout) Cryopreserved Hepatocytes, Mixed Gender	4–8 million viable cells/mL	1.0 mL	TRCS30
Monkey (Cynomolgus) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	MKCS10
Monkey (Cynomolgus) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	MKCS20
Monkey (Cynomolgus) Cryopreserved Hepatocytes, Plateable Male	4–8 million viable cells/mL	1.0 mL	MKCP10
Monkey (Cynomolgus) Cryopreserved Hepatocytes, Plateable Female	4–8 million viable cells/mL	1.0 mL	MKCP20
Mouse (CD-1) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	MSCS10
Mouse (CD-1) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	MSCS20
Mouse (CD-1) Cryopreserved Hepatocytes, Plateable Male	4–8 million viable cells/mL	1.0 mL	MSCP10
Mouse (CD-1) Cryopreserved Hepatocytes, Plateable Female	4–8 million viable cells/mL	1.0 mL	MSCP20
Rabbit (New Zealand White) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	RBCS10
Rabbit (New Zealand White) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	RBCS20
Rabbit (New Zealand White) Cryopreserved Hepatocytes, Plateable Male	4–8 million viable cells/mL	1.0 mL	RBCP10
Rabbit (New Zealand White) Cryopreserved Hepatocytes, Plateable Female	4–8 million viable cells/mL	1.0 mL	RBCP20
Rat (Sprague-Dawley) Cryopreserved Hepatocytes, Male	4–8 million viable cells/mL	1.0 mL	RTCS10
Rat (Sprague-Dawley) Cryopreserved Hepatocytes, Female	4–8 million viable cells/mL	1.0 mL	RTCS20
Rat (Sprague-Dawley) Cryopreserved Hepatocytes, Plateable Male	4–8 million viable cells/mL	1.0 mL	RTCP10
Rat (Sprague-Dawley) Cryopreserved Hepatocytes, Plateable Female	4–8 million viable cells/mL	1.0 mL	RTCP20

Hepatic Products List

Fresh primary hepatocytes (exclusive to North America)

- Extensive tissue sourcing network ensures regular availability of human hepatocytes
- Pre-scheduled animal isolations make it easy to plan your *in vitro* experiments
- Large selection of collagen-coated plating formats, including overlays
- Experienced isolationists provide consistent, high quality lots of hepatocytes

Product	Concentration	Quantity	Cat. no.
Human and animal fresh suspension hepatocytes (Note: There is a minimum order of 15 million cells for freshly isolated suspension hepatocytes.)			
Human Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	HMF501
Dog (Beagle) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	DGFS01
Monkey (Cynomolgus) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	MKFS01
Monkey (Rhesus) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	RHFS01
Mouse (CD-1) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	MSFS01
Mouse (Balb/C) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	BCFS01
Rat (Sprague-Dawley) Fresh Hepatocytes, Suspension	1 million viable cells/mL	1 million cells	RTFS01
Human and animal fresh plated hepatocytes			
Human Fresh Hepatocytes	—	1 x 6-well plate	HMFN06
Human Fresh Hepatocytes	—	1 x 12-well plate	HMFN12
Human Fresh Hepatocytes	—	1 x 24-well plate	HMFN24
Human Fresh Hepatocytes	—	1 x 48-well plate	HMFN48
Human Fresh Hepatocytes	—	1 x 96-well plate	HMFN96
Human Fresh Hepatocytes, with Geltrex™ Overlay	—	1 x 6-well plate	HMFY06
Human Fresh Hepatocytes, with Geltrex™ Overlay	—	1 x 12-well plate	HMFY12
Human Fresh Hepatocytes, with Geltrex™ Overlay	—	1 x 24-well plate	HMFY24
Human Fresh Hepatocytes, with Geltrex™ Overlay	—	1 x 48-well plate	HMFY48
Human Fresh Hepatocytes, with Geltrex™ Overlay	—	1 x 96-well plate	HMFY96
Human Fresh Hepatocytes	—	1 x T75 flask	HMFN75
Dog (Beagle) Fresh Hepatocytes	—	1 x 6-well plate	DGFN06
Dog (Beagle) Fresh Hepatocytes	—	1 x 12-well plate	DGFN12
Dog (Beagle) Fresh Hepatocytes	—	1 x 24-well plate	DGFN24
Dog (Beagle) Fresh Hepatocytes	—	1 x 48-well plate	DGFN48
Dog (Beagle) Fresh Hepatocytes	—	1 x 96-well plate	DGFN96
Dog (Beagle) Fresh Hepatocytes, with Matrigel™ Overlay	—	1 x 6-well plate	DGFY06
Dog (Beagle) Fresh Hepatocytes, with Matrigel™ Overlay	—	1 x 12-well plate	DGFY12
Dog (Beagle) Fresh Hepatocytes, with Matrigel™ Overlay	—	1 x 24-well plate	DGFY24
Dog (Beagle) Fresh Hepatocytes, with Matrigel™ Overlay	—	1 x 48-well plate	DGFY48
Dog (Beagle) Fresh Hepatocytes, with Matrigel™ Overlay	—	1 x 96-well plate	DGFY96
Dog (Beagle) Fresh Hepatocytes	—	1 x T75 flask	DGFN75
Monkey (Cynomolgus) Fresh Hepatocytes	—	1 x 6-well plate	MKFN06
Monkey (Cynomolgus) Fresh Hepatocytes	—	1 x 12-well plate	MKFN12
Monkey (Cynomolgus) Fresh Hepatocytes	—	1 x 24-well plate	MKFN24
Monkey (Cynomolgus) Fresh Hepatocytes	—	1 x 48-well plate	MKFN48

Hepatic Products List

Fresh primary hepatocytes (exclusive to North America) cont.

Product	Concentration	Quantity	Cat. no.
Human and animal fresh plated hepatocytes, cont.			
Monkey (Cynomolgus) Fresh Hepatocytes	----	1 x 96-well plate	MKFN96
Monkey (Cynomolgus) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 6-well plate	MKFY0
Monkey (Cynomolgus) Fresh Hepatocytes, with Geltrex™ Overlay	----	1 x 12-well plate	MKFY12
Monkey (Cynomolgus) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 24-well plate	MKFY24
Monkey (Cynomolgus) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 48-well plate	MKFY48
Monkey (Cynomolgus) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 96-well plate	MKFY96
Monkey (Cynomolgus) Fresh Hepatocytes	---	1 x T75 flask	MKFN75
Mouse (CD-1) Fresh Hepatocytes	---	1 x 6-well plate	MSFN06
Mouse (CD-1) Fresh Hepatocytes	---	1 x 12-well plate	MSFN12
Mouse (CD-1) Fresh Hepatocytes	---	1 x 24-well plate	MSFN24
Mouse (CD-1) Fresh Hepatocytes	----	1 x 48-well plate	MSFN48
Mouse (CD-1) Fresh Hepatocytes	---	1 x 96-well plate	MSFN96
Mouse (CD-1) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 6-well plate	MSFY06
Mouse (CD-1) Fresh Hepatocytes, with Geltrex™ Overlay	----	1 x 12-well plate	MSFY12
Mouse (CD-1) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 24-well plate	MSFY24
Mouse (CD-1) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 48-well plate	MSFY48
Mouse (CD-1) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 96-well plate	MSFY96
Mouse (CD-1) Fresh Hepatocytes	---	1 x T75 flask	MSFN75
Rat (Sprague-Dawley) Fresh Hepatocytes	---	1 x 6-well plate	RTFN06
Rat (Sprague-Dawley) Fresh Hepatocytes	----	1 x 12-well plate	RTFN12
Rat (Sprague-Dawley) Fresh Hepatocytes	---	1 x 24-well plate	RTFN24
Rat (Sprague-Dawley) Fresh Hepatocytes	---	1 x 48-well plate	RTFN48
Rat (Sprague-Dawley) Fresh Hepatocytes	---	1 x 96-well plate	RTFN96
Rat (Sprague-Dawley) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 6-well plate	RTFY06
Rat (Sprague-Dawley) Fresh Hepatocytes, with Geltrex™ Overlay	----	1 x 12-well plate	RTFY12
Rat (Sprague-Dawley) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 24-well plate	RTFY24
Rat (Sprague-Dawley) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 48-well plate	RTFY48
Rat (Sprague-Dawley) Fresh Hepatocytes, with Geltrex™ Overlay	---	1 x 96-well plate	RTFY96
Rat (Sprague-Dawley) Fresh Hepatocytes	---	1 x T75 flask	RTFN75

Hepatic Products List

Liver microsomes and other subcellular fractions

- Animal and human liver subcellular fractions are available as single donors as well as convenient, ready-to-use, pooled lots
- Produced in large pooled lots for reproducible, long-term studies
- Microsomes functionally tested for select CYP450 and Phase II enzyme activities

Product	Concentration	Quantity	Cat. no.
Human and animal liver microsomes			
Human Microsomes, 50 Donors	20 mg/mL	0.5 mL	HMMCPL
Human Microsomes, Pooled Male Donors	20 mg/mL	0.5 mL	HMMCPM
Human Microsomes, Pooled Female Donors	20 mg/mL	0.5 mL	HMMCPF
Human Microsomes, Single Donor	20 mg/mL	0.5 mL	HMMCSD
Human Microsomes, Pediatric Donors	20 mg/mL	0.5 mL	HMMCPe
Human Microsomes, Low Activity Donors	20 mg/mL	0.5 mL	HMMCLO
Human Microsomes, Obese Donors	20 mg/mL	0.5 mL	HMMCOB
Human Microsomes, Morbidly Obese Donors	20 mg/mL	0.5 mL	HMMCMO
Human Microsomes, Overweight Donors	20 mg/mL	0.5 mL	HMMCOw
Human Microsomes, Ideal Weight Donors	20 mg/mL	0.5 mL	HMMCiw
Human Microsomes, Over 75 Years Old Donors	20 mg/mL	0.5 mL	HMMC75
Human Microsomes, 18-39 Years Old Donors	20 mg/mL	0.5 mL	HMMC18
Human Microsomes, 40-60 Years Old Donors	20 mg/mL	0.5 mL	HMMC40
Human Microsomes, High 3A4 Activity Donors	20 mg/mL	0.5 mL	HMMC3A
Human Microsomes, High 2D6 Activity Donors	20 mg/mL	0.5 mL	HMMC2D
Dog (Beagle) Microsomes	20 mg/mL	0.5 mL	DGMCPL
Monkey (Cynomolgus) Microsomes	20 mg/mL	0.5 mL	MKMCPL
Monkey (Rhesus) Microsomes	20 mg/mL	0.5 mL	RHMCPL
Mouse (Balb/C) Microsomes	20 mg/mL	0.5 mL	BCMCPPL
Mouse (CD-1) Microsomes	20 mg/mL	0.5 mL	MSMCPPL
Rat (Sprague-Dawley) Microsomes	20 mg/mL	0.5 mL	RTMCPPL
Mouse (CD-1) Control for Induced Microsomes, Corn Oil Vehicle	20 mg/mL	0.5 mL	MSMCCV
Mouse (CD-1) Microsomes, Induced with 3-Methylcholanthrene	20 mg/mL	0.5 mL	MSMCMC
Mouse (CD-1) Microsomes, Induced with Phenobarbital	20 mg/mL	0.5 mL	MSMCPB
Mouse (CD-1) Microsomes, Induced with Pregnenolone-16 Carbonitrile	20 mg/mL	0.5 mL	MSMCPc
Mouse (CD-1) Microsomes, Induced with Clofibrate	20 mg/mL	0.5 mL	MSMCCI
Fish (Rainbow Trout) Microsomes, Male	20 mg/mL	0.5 mL	TRMC01
Fish (Rainbow Trout) Microsomes, Female	20 mg/mL	0.5 mL	TRMC02
Human and animal S9 fractions			
Human S9 Fractions, Pooled	20 mg/mL	1.0 mL	HMS9PL
Human S9 Fractions, Single Donor	20 mg/mL	1.0 mL	HMS9SD
Dog (Beagle) S9 Fractions	20 mg/mL	1.0 mL	DGS9PL
Fish (Rainbow Trout) S9 Fractions	20 mg/mL	1.0 mL	TRS9PL
Monkey (Cynomolgus) S9 Fractions	20 mg/mL	1.0 mL	MKS9PL
Monkey (Rhesus) S9 Fractions	20 mg/mL	1.0 mL	RHS9PL

Hepatic Products List

Liver microsomes and other subcellular fractions, cont.

Product	Concentration	Quantity	Cat. no.
Human and animal S9 fractions			
Mouse (Balb/C) S9 Fractions	20 mg/mL	1.0 mL	BCS9PL
Mouse (CD-1) S9 Fractions	20 mg/mL	1.0 mL	MSS9PL
Rat (Sprague-Dawley) S9 Fractions	20 mg/mL	1.0 mL	RTS9PL
Human and animal cytosol			
Human Cytosol, Pooled	20 mg/mL	1.0 mL	HMCYPL
Human Cytosol, Single Donor	20 mg/mL	1.0 mL	HMCYSD
Dog (Beagle) Cytosol	20 mg/mL	1.0 mL	DGCYPL
Monkey (Cynomolgus) Cytosol	20 mg/mL	1.0 mL	MKCYPL
Monkey (Rhesus) Cytosol	20 mg/mL	1.0 mL	RHCYPL
Mouse (CD-1) Cytosol	20 mg/mL	1.0 mL	MSCYPL
Mouse (Balb/C) Cytosol	20 mg/mL	1.0 mL	BCCYPL
Rat (Sprague-Dawley) Cytosol	20 mg/mL	1.0 mL	RTCYPL

Hepatocyte media, reagents and kits

- CHRM™ Medium allows you to retain high viabilities while thawing cryopreserved hepatocytes
- Plating Supplement Pack contains media additives to support the thawing and plating of cryopreserved hepatocytes. Plating Supplement Pack includes pre-qualified fetal bovine serum, insulin, dexamethasone, gentamicin, L-glutamine and HEPES to supplement one 500 ml bottle of medium.
- Maintenance Supplement Pack contains media additives to support short-term cultures of primary hepatocytes. Maintenance Supplement Pack includes dexamethasone, ITS+ (insulin, transferrin, selenium complex, BSA and linoleic acid), gentamicin, L-glutamine, and HEPES to support one 500 ml bottle of medium.

Product	Concentration	Quantity	Cat. no.
Media and plates for hepatocyte culture			
Cryopreserved Hepatocytes Recovery Medium (CHRM™)	—	50 mL	CM7000
Plating Supplement Pack for Cryopreserved Hepatocytes (Serum-containing)	—	1 kit, for 500 mL medium	CM3000
Maintenance Supplement Pack for Cryopreserved Hepatocytes (Serum-free)	—	1 kit, for 500 mL medium	CM4000
Cryopreserved Hepatocytes Plating Medium (CHPM)	—	50 mL	CM9000
Cryopreserved Hepatocyte Evaluation Kit, for use with one vial of cryo hepatocytes	—	1 kit	CM8000
Collagen-Coated Plate	—	1 x 6-well	CM1006
Collagen-Coated Plate	—	1 x 12-well	CM1012
Collagen-Coated Plate	—	1 x 24-well	CM1024
Collagen-Coated Plate	—	1 x 48-well	CM1048
Collagen-Coated Plate	—	1 x 96-well	CM1096
Plate Lid	—	1 lid	CM1002

Hepatic Products List

GenoMembrane™ transporter reagents (available in North America and Europe)

- Wide selection of major ABC efflux transporter membranes and vesicles
- Straightforward *in vitro* screening for drug candidates' substrate and interaction potential
- High signal-to-background ratios

Product	Concentration	Quantity	Cat. no.
GenoMembrane™ assay reagents			
ABC Transporter ATPase Assay Reagent Kit	—	160 assays	GM3020
BSEP Vesicular Transport Assay Reagent Set	—	100 assays	GM3001
MDR1 Vesicular Transport Assay Reagent Set	—	100 assays	GM3030
Vesicular Transport Assay Reagent Set for MRP1, MRP2, MRP3, MRP4, MRP8, BCRP	—	100 assays	GM3010
GenoMembrane™ ABC transporter membranes (Each vial contains enough membranes for up to 125 ATPase assays.)			
Human MDR1 Membranes	5 mg/mL	0.5 mL	GM0015
Human MRP1 Membranes	5 mg/mL	0.5 mL	GM0010
Human MRP2 Membranes	5 mg/mL	0.5 mL	GM0001
Dog (Beagle) MRP1 Membranes	5 mg/mL	0.5 mL	GM0017
Dog (Beagle) MRP2 Membranes	5 mg/mL	0.5 mL	GM0014
Monkey (Cynomolgus) MRP2 Membranes	5 mg/mL	0.5 mL	GM0018
Mouse (Balb/C) MDR1a Membranes	5 mg/mL	0.5 mL	GM0004
Mouse (Balb/C) MDR1b Membranes	5 mg/mL	0.5 mL	GM0016
Rat (Sprague-Dawley) MRP1 Membranes	5 mg/mL	0.5 mL	GM0011
Rat (Sprague-Dawley) MRP2 Membranes	5 mg/mL	0.5 mL	GM0002
Control ABC Transporter Membranes	5 mg/mL	0.5 mL	GM0003
GenoMembrane™ ABC transporter vesicles (Each vial contains enough vesicles for up to 50 vesicular transport assays.)			
Human BCRP Vesicles	5 mg/mL	0.5 mL	GM0008V
Human BSEP Vesicles	5 mg/mL	0.5 mL	GM0005V
Human MDR1 Vesicles, with fluorescent substrate N-methylquinidine	5 mg/mL	0.5 mL	GM0015HV
Human MRP1 Vesicles	5 mg/mL	0.5 mL	GM0010V
Human MRP2 Vesicles	5 mg/mL	0.5 mL	GM0001V
Human MRP3 Vesicles	5 mg/mL	0.5 mL	GM0021V
Human MRP4 Vesicles	5 mg/mL	0.5 mL	GM0012V
Human MRP8 Vesicles	5 mg/mL	0.5 mL	GM0013V
Dog (Beagle) BSEP Vesicles	5 mg/mL	0.5 mL	GM0019V
Dog (Beagle) MRP1 Vesicles	5 mg/mL	0.5 mL	GM0017V
Dog (Beagle) MRP2 Vesicles	5 mg/mL	0.5 mL	GM0014V
Monkey (Cynomolgus) MRP2 Vesicles	5 mg/mL	0.5 mL	GM0018V
Mouse (Balb/C) MDR1a Vesicles, with fluorescent substrate	5 mg/mL	0.5 mL	GM0004HY
Mouse (Balb/C) MRP2 Vesicles	5 mg/mL	0.5 mL	GM0022V
Rat (Sprague-Dawley) BCRP Vesicles	5 mg/mL	0.5 mL	GM0007V
Rat (Sprague-Dawley) BSEP Vesicles	5 mg/mL	0.5 mL	GM0006V
Rat (Sprague-Dawley) MRP1 Vesicles	5 mg/mL	0.5 mL	GM0011V
Rat (Sprague-Dawley) MRP2 Vesicles	5 mg/mL	0.5 mL	GM0002V
Rat (Sprague-Dawley) MRP4 Vesicles	5 mg/mL	0.5 mL	GM0020V
Control ABC Transporter Vesicles	5 mg/mL	0.5 mL	GM0003V
Control MDR1 Vesicles	5 mg/mL	0.5 mL	GM0003HY

Hepatic Products List

B-CLEAR® hepatic transport kits (available in North America)

- Kit formats to determine the hepatobiliary disposition of drug candidates
- Provides an *in vitro* hepatocyte model which correlates to *in vivo* function
- Facilitates assessment of potential for hepatic transporter-mediated drug interactions

Product	Concentration	Quantity	Cat. no.
B-CLEAR® hepatic transport kits (All kits contain fresh primary hepatocytes, media, buffers and control plates.)			
B-CLEAR® Human Hepatic Transport Kit	-	6 x 6-well plates	BCHM06
B-CLEAR® Human Hepatic Transport Kit	-	3 x 24-well plates	BCHM24S
B-CLEAR® Human Hepatic Transport Kit	-	6 x 24-well plates	BCHM24L
B-CLEAR® Rat Hepatic Transport Kit	-	6 x 6-well plates	BCRT06
B-CLEAR® Rat Hepatic Transport Kit	-	6 x 24-well plates	BCRT24


www.invitrogen.com

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E.3

PRODUCT CHARACTERIZATION SHEET**LOT #: HuP58***(Human Cryopreserved Hepatocytes)*

APPLICATION RECOMMENDATIONS										
Metabolic Stability/Profiling Studies using Cell Suspensions							Recommended			
INVENTORY INFORMATION										
Number of Vials Produced							469			
Current Available inventory							460			
DONOR DEMOGRAPHICS										
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Male	Caucasian	39	32	No	No	No	None	CMV+	GSW to Head
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Male	Caucasian	41	35	Yes	Heavy	Yes	None	CMV+	ICH
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Male	Caucasian	56	29	No	Social	No	None	CMV+	Head Trauma
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Male	Caucasian	59	26	No	Yes	No	None	All Negative	CVA
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Male	Caucasian	20	12	No	No	No	None	CMV+	Anoxia
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Female	Caucasian	18	15	No	No	No	None	All Negative	CNS Tumor
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Female	Caucasian	17	18	No	No	No	None	All Negative	Head Trauma
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Female	Caucasian	26	26	Yes	Social	No	Opiates, Effexor	CMV+	Head Trauma
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Female	Caucasian	53	28	No	No	No	None	CMV+	CVA
Species	Sex	Race	Age	BMI	Smoker	Alcohol Use	Drug Use	Medications	Serological Data	Cause of Death
Human	Female	Caucasian	17	23	Yes	Social	Marijuana	Lexapro	CMV+	Head Trauma

#1 POST THAW VIABILITY & CELL QUALITY ASSESSMENT

THAWING MEDIUM USED	OPTIMAL CETRIFUGE CONDITIONS	% VIABILITY (POST THAW)	VIABLE CELL YIELD PER VIAL	VIABILITY STABILITY (% VIABILITY OF SUSPENSION AFTER 2 HOURS INCUBATION)
CHRM	76g X 6 minutes @ room temperature	81%	5.8 million	71

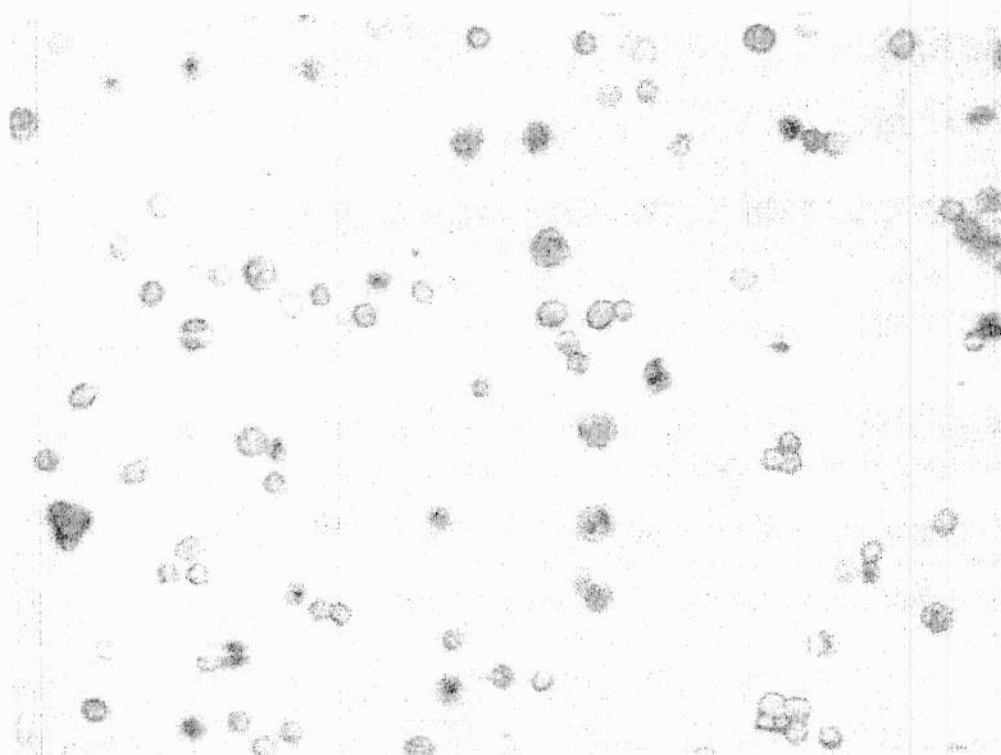
#2 POST THAW VIABILITY & CELL QUALITY ASSESSMENT

THAWING MEDIUM USED	OPTIMAL CETRIFUGE CONDITIONS	% VIABILITY (POST THAW)	VIABLE CELL YIELD PER VIAL	VIABILITY STABILITY (% VIABILITY OF SUSPENSION AFTER 2 HOURS INCUBATION)
WEM	100g X 10 minutes @ room temperature	75%	8.3	61%

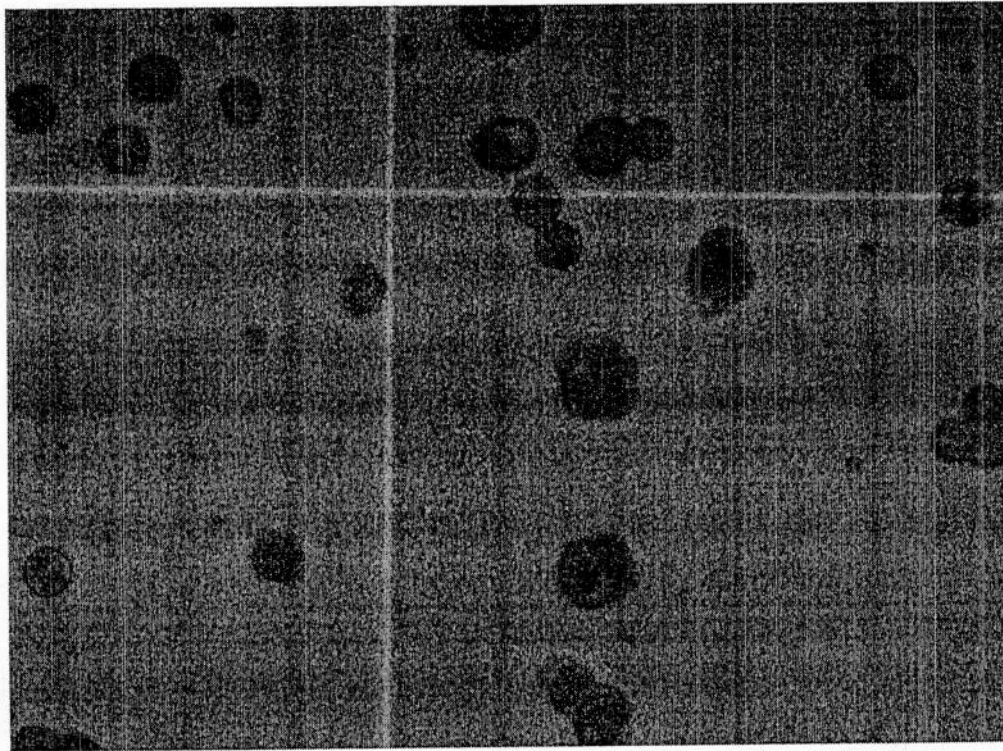
METABOLIC PROFILE (pmol/1 x 10⁶ cells/min)

CYP 3A4	CYP 1A2	CYP 2C8	CYP 2C9	CYP 2C19	CYP 2D6
567	38	34.4	83.3	82	15.6
7-Ethoxycoumarin-O-deethylase (ECOD)		7-Hydroxycoumarin Glucuronidation (Phase II)		7-Hydroxycoumarin Sulfation (Phase II)	
21.4		600		33.2	

Post Thaw 10x magnification(WEM)



Post Thaw 20x magnification (WEM)



2 hours after thawing (WEM)



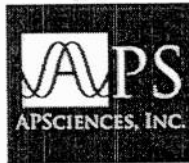
METABOLIC ACTIVITY

The commonly tested Phase I (P450) and Phase II (UGT, SULT) drug metabolizing enzymes were analyzed for activity in HuP50. Cells were carefully thawed in and resuspended in Dulbecco's Modified Eagles Medium DMEM (serum-free). The cell suspension was aliquoted at 0.5×10^6 cells/well into a 24-well non-coated plate containing the appropriate substrate and placed in a humidified incubator at 37°C, 95% relative humidity, 5% CO₂ on an orbital shaker. At the appropriate time point for each substrate, a sample was collected from each well and stored frozen at -70°C until it was processed by LC-MS/MS or HPLC analysis. Metabolite formation was measured by standard biochemical assays using GLP validated LC-MS/MS assays. At least six calibration standards and 12 quality control samples (at three different concentrations) were used to evaluate the quality of the analytical runs.

Substrate Probes to Assess Human CYP450 Metabolic Activity.

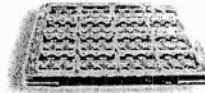
ENZYME	SUBSTRATE	CONCENTRATION	INCUBATION TIME	MARKER METABOLITE
CYP1A2	Phenacetin	100 µM	15 min	Acetaminophen
CYP2B6	Bupropion	500 µM	15 min	Hydroxybupropion
CYP2C8	Paclitaxel	20 µM	45 min	6α-Hydroxypaclitaxel
CYP2C9	Diclofenac	25 µM	15 min	4'-Hydroxydiclofenac
CYP2C19	(S)-Mephenytoin	250 µM	30 min	4'-Hydroxymephenytoin
CYP2D6	Detromethorphan	15 µM	15 min	Dextrorphan
CYP3A4	Testosterone	200 µM	15 min	6β-Hydroxytestosterone
CYP3A4	Midazolam	10 µM	10 min	1-hydroxymidazolam
Phase I	7-Ethoxycoumarin	100 µM	30 min	(ECOD) 7-Hydroxycoumarin (7-HC)
Phase II	7-Hydroxycoumarin	100 µM	30 min	7-Hydroxycoumarin Glucuronide (7-HCG) and 7-Hydroxycoumarin Sulfate (7-HCS)

E.4



APSciences Proudly Presents...

IdMOC TECHNOLOGY



New technology for advanced research needs. The Integrated Multiple Organ Culture plate (IdMOC) provides a method to model in vivo multiple-organ interaction in vitro. [CLICK HERE TO LEARN MORE](#)

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HUMAN HEPATOCYTES

Higher expectations = Better results. APSciences has taken the guesswork out of the selection of high quality cryopreserved Human Hepatocytes. As the exclusive manufacturing partner of Invitrogen CellDirect, our cryopreserved hepatocytes are produced under strict isolation procedures to ensure only the best cells are cryopreserved in each vial. This adherence to strict quality standards yields cells with high viability and differentiated functions for all of your research needs.

Cryopreserved Hepatocytes are available in single, pooled and plateable versions. Average yield is 5 million cells/ vial. Contact us for assistance in lot selection.*

For all orders and inquiries, please contact info@apsciences.com

* APSciences manufactures the 4000 lot series. We will work with you to select the best lots for your application. Ordering is processed through Invitrogen CellDirect.

AVAILABLE FORMATS

Description/Quantity

Cryopreserved Human Hepatocytes, Male/ea
Cryopreserved Human Hepatocytes, Female/ea

Cryopreserved Human Hepatocytes, 10 Donor Pool, Male/ea
Cryopreserved Human Hepatocytes, 10 Donor Pool, Female/ea

Cryopreserved Human Hepatocytes, Plateable, Male/ea
Cryopreserved Human Hepatocytes, Plateable, Female/ea

[BACK TO PRODUCTS & SERVICES](#)

E.5

CellzDirect, Inc. enters into 5 year exclusive partnership with Advanced Pharmaceutical Sciences, Inc.

Press Release, September 14, 2006

CellzDirect Inc. (CDI), a global leader in hepatic cell products and in vitro contract services, has entered into a long-term, exclusive strategic partnership with Advanced Pharmaceutical Sciences, Inc. (APS). Under the agreement, APS will focus exclusively on producing cryopreserved human hepatocytes to supplement CellzDirect's hepatic products inventory. CellzDirect will serve as an exclusive distributor for APS's new medium for thawing cryopreserved hepatocytes (cryopreserved hepatocyte recovery medium) which, when used with the CDI/APS cryopreserved hepatocytes, yield cells with high viability and attachment efficiency.

The goal of the collaboration is to meet the growing demand for high-quality cryopreserved human hepatocytes, especially "attachable" cryopreserved human hepatocytes needed for enzyme induction, drug transporter, and in vitro hepatotoxicity screening studies in the pharmaceutical industry. The FDA recently accepted the use of attachable cryopreserved human hepatocytes for use in enzyme induction drug-drug interaction studies.

APS is headed by President and CEO Dr. Albert P. Li, a leading researcher and pioneer in hepatocyte isolation and cryopreservation.

"We are thrilled to partner with Dr. Li and his team at APS," said Scott Edelman, President and CEO of CellzDirect, Inc. "Our combined scientific expertise with hepatocytes and strong commitment to making highquality human hepatocytes more readily available promises to have a profound affect on *in vitro* research."

"We are extremely excited about our new technologies that allow us to routinely produce cryopreserved hepatocytes with the attachment efficiency, morphology, and biochemical properties of freshly isolated cells," said Dr. Li. "The quality of our new cryopreserved human hepatocyte lots is already being touted as the new standard for industry. The partnership with CellzDirect will allow us to provide these pristine cells to researchers around the world."

For more information on cryopreserved and other hepatic products, contact CellzDirect's sales team at 1-866-95-CELLZ (1-866-952-3559), or stop by the CellDirect booth at the upcoming International Society for the Study of Xenobiotics (ISSX) in Puerto Rico on October 23-26.

About CellzDirect: CellzDirect, Inc., is a privately held bioscience company that provides bio-pharmaceutical companies with quality cell products and contract laboratory services focused primarily on drug metabolism and toxicology. With CellzDirect's support, scientists are better able to conduct research that accelerates the discovery of safe and effective drugs.

For further information about CellzDirect, please contact:

Shiloh Barfield, Director of Sales and Marketing, CellzDirect, Inc.

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Email: shilohb@cellzdirect.com